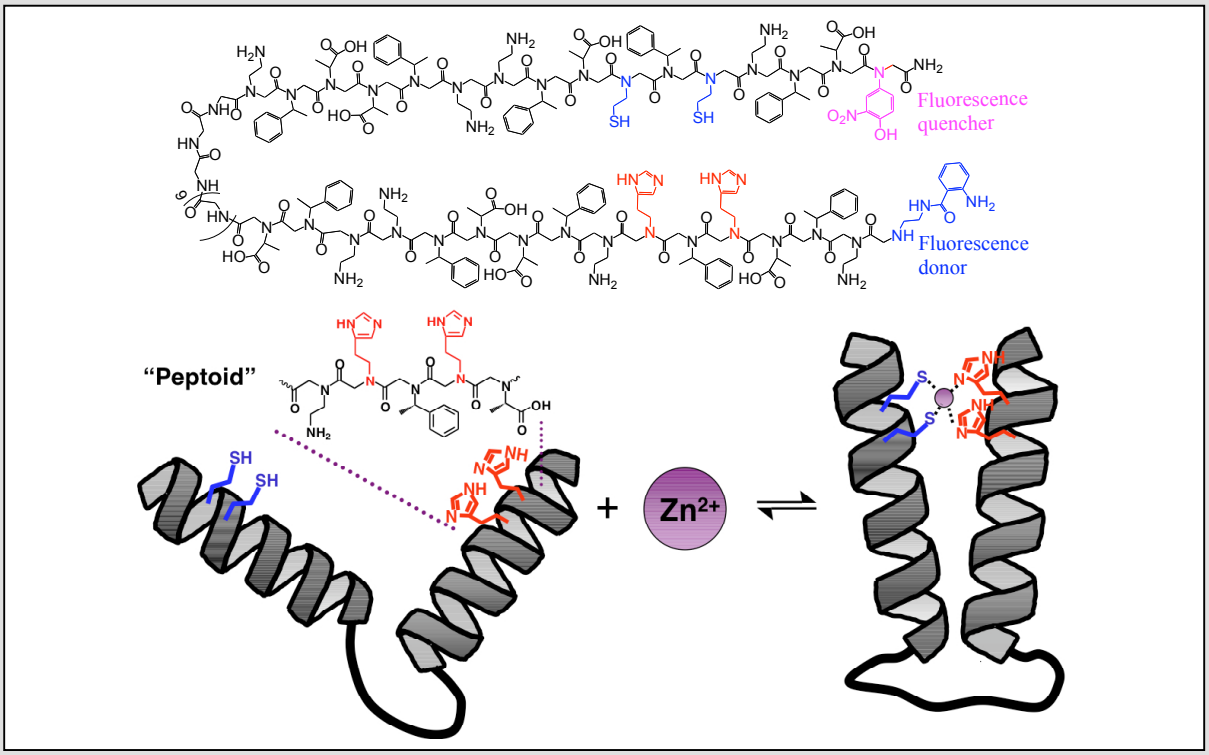
Protein Mimetics based on Bio-inspired Peptoid Polymers

Byoung-Chul Lee[1], Tammy K. Chu[1], Ken A. Dill[2], and Ronald N. Zuckermann[1]

[1]Biological Nanostructures Facility, The Molecular Foundry, Lawrence Berkeley National Laboratory, 1 Cyclotron Road, Berkeley, California 94720
[2]Graduate group in Biophysics and Department of Pharmaceutical Chemistry, 600 16th Street, University of California, San Francisco, California 94143

Folded polymeric peptoid nanostructures bind metal ions with sub-nanomolar affinity

A synthetic peptoid with two helices has been folded into a protein-like tertiary structure that displays thiol and imidazole functional groups at defined positions in space.



A fundamental challenge in nanoscience is creating materials with atomic level precision over the structure. One way Nature achieves this level of control is by folding linear polymer chains into precise 3D shapes. We are mimicking this design principle with completely non-natural polymers called peptoids.

Peptoids are a novel class of non-natural biopolymer based on an N-substituted glycine have many unique properties that bridge the gap between proteins and bulk polymers. Like proteins, they are a sequence-specific heteropolymer, capable of folding into specific shapes and exhibiting potent biological activities; and like bulk polymers they are chemically and biologically stable and relatively cheap to make. Peptoids are efficiently assembled via automated solid-phase synthesis from hundreds of chemically diverse building blocks allowing the rapid generation of huge combinatorial libraries.

Here, a two-helix bundle was designed and synthesized that displays metal-binding residues in the proper orientation to create a selective and high-affinity zinc ion binding site. This work is the first example of a non-natural polymer with a defined tertiary structure and a protein-like function.

Reference: *J. Am. Chem. Soc.* **130**, 8847 (2008).